a total of 474, 456, 443, 421, and 370 subjects completed the 1st, 2nd, 3rd, 4th, and 5th yr study, respectively. At the end of each year, samples were analyzed from those subjects with protocol-defined HBV DNA breakthrough (increase $\geq$ 1.0 log10 copy/ml from the treatment nadir) for the rtN236T or rtA181V ADV mutations associated with in vitro ADV resistance. ADV was associated with a low rate of resistance, cumulative rate of 0% after 1 year,1.3% after 2 years, 5.4% after 3 years and 10.4% after 4 years, 14.6% after 5 years.
Our data showed that treatment with ADV in Chinese HBeAg positive CHB subjects for up to 5 years resulted in a cumulative rate of 14.6% (70/480) ADV resistance-associated mutations with HBV DNA breakthrough.

Concurrent Session 10 – Use and Abuse of Antibiotics

CS10-01 The Role of Infectious Disease Physician in the Rational Use of Antibiotics

Yonghong Xiao*. *First Hospital, Peking University, Beijing, China*

Antibacterial agents are the most common used drug in daily clinical practice, in which the wide application and high requirement for professional capability often leads irrational prescription. The professionals are urgent need for promoting antibiotic use. Infectious disease physicians should take the key role in the work because:

1. Infectious doctors holding professional priority:
   a. One of the responsibilities endue with infectious doctor is therapy of infections;
   b. Antibiotic is the major therapeutic measure for infectious doctor;
   c. Infectious doctors are familiar with all the basic information related with infection and chemotherapy, such as bacteriology, virology and antibiotics;
   d. Infectious doctors are in the center for contacting pharmacist, microbiologist and nosocomial infection controller.
2. Infectious doctors should do following effect to conduct the work well:
   a. Affluent experience in diagnosis and treatment of infectious diseases;
   b. Substantial basic medical knowledge, such as epidemiology, bacteriology, pathogenesis, pathology, etc;
   c. Catching up with new information concerning with their occupation, such as bacterial resistance, new antibacterial therapeutic strategy, etc;
   d. Familiar with all the information of antibacterial agents, such as pharmacodynamics, pharmacokinetics, dosing, side effect, indications, etc.
3. Infectious doctors should take the role by:
   a. Collaboration with their clinical co-workers in other fields;
   b. Collaboration with pharmacist, microbiologist and hospital manager;
   c. Active participation for clinical consulting;
   d. Personal professional improvement;
   e. Holding education and training in hospital about antibacterial rational use;
   f. Conducting clinical and basic researches.

CS10-02 Antibiotic and Antifungal Resistance in Antibiotic "Free" Environment

V. Krcmery*, E. Kalavsky. *St. Elizabeth University College of Health and Social Sciences, Laboratory of Tropical Diseases, Slovakia*

It is widely accepted that in community antibiotic/antifungal resistance is related with consumption. One of the arguments "pro" is reversibility of resistance which happens frequently in hospital but was detected also in the community level in at least 3 countries (Denmark, Iceland and Finland).
As every rule is confirmed by an exception, here are several examples of antimicrobial resistance in regions with no or very little antimicrobial pressure. We have observed and published data on absence of resistance to penicillin, oxacillin and erythromycin in *S. pneumoniae* and *S. aureus* in an area isolated 21 years by civil war in southern Sudan with no communication, no health infrastructure and no antimicrobial drugs on the market however among the same patients 80% tetracycline resistance in viridans streptococci was observed.
We have observed 66-75% ceftazidim resistance in *Enterobacter* spp. Isolated from Cambodian HIV positive children living in rural areas where no antibiotic drugs are accessible. Last year a report on high quinolone resistance in *E. coli* from indigenous Indian population in rural Bolivia was published by Bartoloni et al. Similar situation was observed among inhabitants of very isolated villages from Amazon basin in Peru and Bolivia. Shahum et al. described 8 children infected with voriconazol resistant *Candida* spp. strains from rain forest rural area of Cambodia near Viet Nam border. Those children and their parents never received according to patient's history and medication for years. Other two similar observations are coming from Nepal and French Guyana. Those at least 7 reports does no weak our conclusion that consumption of antibiotics is a major driver of antimicrobial resistance in the community. However findings from southern Sudan, Cambodia, Peru and Bolivia indicate that other factors promoting antimicrobial resistance in absence of antimicrobial pressure should be studied as well.

CS10-03 Antibiotic Resistance and the Role of Antibiotic Stewardship

Victor Lim*. *International Medical University, Kuala Lumpur, Malaysia*

The discovery of antibiotics is one of the most significant event in medical history. Antibiotics have added a decade to the average life expectancy. Together with vaccination, clean water and other public health measures, mortality from infectious diseases was dramatically reduced. There was great optimism in the 1950s and 1960s that infectious diseases were no longer a major challenge. Unfortunately this optimism was unfounded due to various reasons including the emergence of antibiotic resistance. Resistance is not new. Sir Alexander Fleming, the discoverer of penicillin said in his Nobel Prize Address in 1945 that, "It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body."
The resistome is the collection of all the antibiotic resistance genes and their precursors both in pathogenic and non-pathogenic bacteria. Studies of the soil resistome has revealed antibiotic resistant genes to a wide variety of antibiotics including synthetic compounds like quinolones and newer antimicrobials like Synercid and daptomycin despite no known prior exposure to these antibiotics or their analogues. The development of antimicrobial resistance had therefore been going on in nature long before antibiotics came into medicinal use. A recent study has also shown that bacteria can subsist on antibiotics as their sole carbon source. The soil resistome therefore constitute an unappreciated reservoir that can contribute to increasing resistance in pathogenic bacteria
Antibiotic resistance is a major challenge world-wide. It occurs in gram positive as well in gram negative organisms and in healthcare associated as well as in community acquired infections. In the last two decades only 2 new classes of anti-bacterials (the oxazolidinones and the lipopeptides) have been introduced for clinical use. The situation is now so dire that some physicians have predicted that there will not be any effective antibiotics to treat seriously ill patients in the near future.

There is a close association between overuse of antibiotics and emergence of resistance. Surveys worldwide point to a high prevalence of inappropriate antibiotic use both in hospital based or community based studies. Inappropriate use is common in developed as well as developing countries. Overuse of antibiotics exerts a selection pressure hence changing a largely susceptible population of organisms to a largely resistant one. Although antibiotic resistance has a fitness cost, compensatory mutations can mitigate this fitness cost.
Stewardship is the careful and responsible management of something entrusted to one's care. Antibiotic stewardship is now an important public health function as antibiotic resistance has become one of the most important clinical challenges today.
Antibiotic stewardship should be practiced at international, national and institutional levels. At the international level the World Health Organisation has played a key role in encouraging all countries to adopt national strategies to contain antibiotic resistance. A national strategy should be a multi-faceted approach which includes strengthening antibiotic resistance surveillance, developing and implementing antibiotic guidelines for practitioners, improving access to and upgrading the quality of microbiological diagnostic facilities, increasing public awareness of antibiotic resistance and controlling and regulating the use of antibiotics for both medicinal and non-medicinal purposes.
In Malaysia the Ministry of Health has established a fairly well defined administrative structure for the purpose of antibiotic stewardship. The National Infection and Antibiotic Control Committee is chaired by the Director General of Health. A National Antibiotic Resistance Surveillance System was established in 1990. The monitoring of antibiotic utilization is also undertaken and two National Medicines Use surveys has thus far been completed. Monitoring of antibiotic utilisation in the Ministry of Health state hospitals is focused on 4 major groups of compounds namely cephalosporins, carbapenems, quinolones and glycopeptides.
At the institutional level all government hospitals have antibiotic formularies and guidelines. However the effectiveness of antibiotic stewardship at an institution depends very much on the presence of "champions". In the private sector doctors can use any product so long as it is registered by the Drug Control Authority and consultants operate as independent contractors in private hospitals. Professional societies also issue practice guidelines from time to time but the effectiveness of these guidelines is questionable.
Other measures in antibiotic stewardship would be the legislative control of prescription and sales of antibiotics for medicinal use as well as non-medicinal use and the regulation of marketing and promotional activities by pharmaceutical companies.
The emergence of resistance is threatening the usefulness of antibiotics and there is an urgent need to conserve this precious resource. Antibiotic stewardship is crucial to contain resistance. A concerted effort employing a multifaceted strategy is essential at international, national and institutional levels and all stakeholders need to work together to meet this challenge.

CS10-04 Problems with Empirical Antibiotics in Febrile Neutropenia

B.H. Tan*. *Department of Internal Medicine, Singapore General Hospital, Singapore*

Over the years, numerous well-conducted randomized controlled trials have provided much information guiding the empirical use of antibiotics in febrile antibiotics. Monotherapy with ceftazidime, cefepime, imipenem or meropenem is well supported by the data, and is in common use. At the same time, the more traditional combination of an anti-pseudomonal beta-lactam with an aminoglycoside continues to be used.
Problems with these approaches have arisen largely because of rising antibiotic resistance. Outbreaks of metallo-betalactamase (MBL)-producing organisms have occured in Haematology-Oncology units, as have outbreaks of vancomycin-resistant enterococci (VRE) and *Stenotrophonomas maltophilia*. These outbreaks have been attributed in part to the overuse of antibiotics. There are also problems associated with individual drugs, such as the purported increase in mortality associated with cefepime use, the link between piperacillin-tazobactam and false-positive galactomannan readings, and the link between ceftazidime and the extended-spectrum beta-lactamases (ESBLs).
These topics will be reviewed in the talk.

Concurrent Session 11 – HIV/AIDS

CS11-01 Molecular Epidemiological Study of HIV-1 CRF01_AE Transmission in Hong Kong

Wing Cheong Yam*. *Department of Microbiology, Queen Mary Hospital, The University of Hong Kong, Hong Kong SAR, China*

A total of 465 HIV-1 CRF01_AE *pol* sequences were collected for phylogentic study by the Bayesian coalescent method. CRF01_AE patient population included 363 males (78.1%) and 102 females (21.9%) while 65% (314/465) were local Chinese. Major transmission routes were heterosexual contact (63%), followed by intravenous drug use (19%) and men having sex with men (MSM) (17%). From phylogenetic analysis, local CRF01_AE strains were from multiple origins with 3 separate transmission clusters identified. Cluster 1 consisted mainly of Chinese male intravenous drug users (IDU) and heterosexual. Cluster 2 and 3 included mainly local Chinese MSM and non-Chinese Asian IDUs respectively. Chinese reference isolates available from China (Fujian, Guangxi, or Liaoning) were clonally related to our transmission clusters, demonstrating the epidemiological linkage of CRF01_AE infections between Hong Kong and China. The 3 individual local transmission clusters were estimated to have initiated since late-80s and late-90s, causing subsequent epidemics in the early-2000s. This is the first comprehensive molecular epidemiological study of HIV-1 CRF01_AE in Hong Kong. It revealed MSM contact is becoming a major route of local CRF01_AE transmission in Hong Kong. Epidemiological linkage of CRF01_AE between Hong Kong and China observed in this study indicates the importance of regular molecular epidemiological surveillance for the HIV-1 epidemic in our region.

CS11-02 Clinical Retrospective Study of Haemophilia A Patients with AIDS after Long Term HAART

Hongzhou Lu*. *Division of Infectious Diseases, Fudan University, Shanghai, China*

Objcetive: To observe and evaluate the impact of long term highly active antiretroviral therapy (HAART) in Haemophilia A patients complicated with AIDS (Haemophilia A/AIDS).
Method: 39 Haemophilia A/AIDS patients undergone HAART for 6 years between 1 June 2002 and 31 July 2008 were enrolled. The data of Haemophilia A/AIDS patients' consultation times (times/year), bleeding times (times/year), VIII factor transfusion times (times/year), amount of VIII factor transfusion (U/year) and VIII:C level were analyzed to evaluate haemorrhage status; grade scales were designed to measure the joint function and physical ability. Then the data of HIV virus load and $CD4^+$ cells count were also observed to evaluate the effect of HAART on immune recovery; finally, the data of complete blood cell count, hepatic panel, blood lipid assay, renal function, plasma glucose, uric acid and blood amylase were also observed to evaluate side effect of long term HAART.
Results: After 6 years of HAART, no obvious change could be seen in Haemophilia A/AIDS patients' mean consultation times, mean bleeding times, mean VIII factor transfusion times and mean amount of VIII factor transfusion ($P>0.05$), only one case exhib-